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Hybrid Transureteral Nephrectomy in a Survival Porcine Model

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ABSTRACT

Background and Objectives: Natural-orifice approaches for nephrectomy have included access via the stomach, vagina, bladder, and rectum. Recently, the feasibility of using the ureter as a natural orifice for natural-orifice transluminal endoscopic surgery nephrectomy has been demonstrated in a nonsurvival porcine model. The purpose of this study was to assess the outcomes of transureteral laparoscopic natural-orifice transluminal endoscopic surgery nephrectomy in a survival porcine model.

Methods: Three pigs underwent hybrid transureteral natural-orifice transluminal endoscopic surgery nephrectomy. An experimental balloon/dilating sheath was inserted over a wire to dilate the urethra, ureteral orifice, and ureter. Through a bariatric 12-mm laparoscopic port, the ureter was opened medially and the hilar dissection was performed. Next, 2 needlescopic ports were placed transabdominally to facilitate hilar transection. The kidney was morcellated using a bipolar sealing device and extracted via the ureter using the housing of a bariatric stapling device. The ureteral orifice was closed with a laparoscopic suturing device. The bladder was drained by a catheter for 10 to 14 days postoperatively. Pigs were euthanized on postoperative day 21.

Results: All surgical procedures were successfully completed, with no intraoperative complications. One pig had an episode of postoperative clot retention that resolved with catheter irrigation. Each pig was healthy and eating a normal diet prior to euthanasia.

Conclusions: This study demonstrates the feasibility of a hybrid transureteral approach to nephrectomy in a survival porcine model. This technique avoids the intentional violation of a second organ system and the risk for peritoneal contamination. Improved instrumentation is needed prior to implementation in the human population.

Key Words: Natural-orifice endoscopic surgery, Nephrectomy, Minimally invasive surgery, Investigational therapy.

INTRODUCTION

The notion of transluminal surgery dates back as early as the second century, when Soranus of Ephesus performed a transvaginal hysterectomy.[1] Since the first animal laparoscopic experiment in 1902,[2] ongoing efforts to achieve the "scarless" surgery have been a driving force in the evolution of minimally invasive techniques. The most radical example is natural-orifice transluminal endoscopic surgery (NOTES), which intentionally disrupts a healthy organ to gain access to a diseased organ, thus avoiding incising the abdominal wall. NOTES has been performed successfully in a wide range of abdominal surgical procedures, including cholecystectomy,[3] gastrectomy,[4] peritoneoscopy,[5] and even nephrectomy.[6]

NOTES is currently in the initial stages of development, so there are few reports demonstrating the clinical benefits of this minimally invasive technique. The goal in developing NOTES techniques is that the advantages of traditional laparoscopic surgery (ie, less pain, improved cosmesis, and more rapid return to normal activity) will be magnified in an even less invasive surgery. NOTES nephrectomies have been described through a variety of approaches, including transgastric, transvaginal, and transrectal.[7] Compared with traditional laparoscopic techniques in which skin incisions are used to gain access to the abdomen, these approaches intentionally traverse a hollow viscus of a separate organ system, each with a unique array of microbial colonization. Contamination of the peritoneal cavity with bowel or vaginal flora and the possibility of subsequent infectious complications exist with these approaches.

Recently, our center published the first report of a hybrid transureteral NOTES nephrectomy in a nonsurvival porcine model.[8] This novel NOTES approach does not re-

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quire the intentional violation of a separate organ system as in other approaches. After a careful review of surgical technique and technical modifications, we sought to determine the feasibility of a hybrid transureteral NOTES nephrectomy in a survival porcine model.

METHODS

After approval was obtained from the Institutional Animal Care and Use Committee, 3 female farm pigs were selected for the procedure (weight range, 41–45 kg). The surgical procedures were performed on 3 nonconsecutive days over a 3-week period. All procedures were completed by a single surgeon with fellowship training in minimally invasive and endourologic surgery (D.D.B.). The pigs were given no food or liquid for the 12 hours prior to surgery. General anesthesia was induced with a combination of ketamine (2.2 mg/kg), telazol (4.4 mg/kg), and xylazine (2.2 mg/kg). Anesthesia was maintained using isoflurane (2.5%–3.5%) under the direction of the Institutional Animal Care Facility veterinarian. Intravenous access was established in either the saphenous or ear vein with a 22-gauge angiocatheter. The animals were given lactated Ringer's solution at a rate of 5 mL/kg/h throughout the operation. The pigs were placed in a modified lithotomy position with sterile preparation and draping of the abdomen and perineum.

The procedure was initiated with cystoscopic (17-F rigid cystoscope; Gyrus ACMI, Southborough, Massachusetts) identification of the left ureteral orifice. A 0.038-inch angle-tipped hydrophilic guidewire (Terumo Medical Corporation, Somerset, New Jersey) was then placed to the level of the renal pelvis using a fluoroless technique. Using a 6-F open-ended ureteral catheter (Cook Medical, Bloomington, Indiana), the hydrophilic wire was then exchanged for a 0.038-inch Amplatz extrastiff guidewire (Cook Medical). The bladder was then drained, and a novel integrated balloon dilator and sheath (Terumo Medical Corporation) were placed over the superstiff guidewire **(Figure 1a)**. The urethra, ureteral orifice, and distal ureter (to a distance 2 cm proximal to the ureteral orifice) were then dilated to 33 F by inflating the balloon dilator to 20 atm.

After removal of the dilating balloon, a bariatric 12-mm laparoscopic port with a previously drilled 5-F hole at the tip of the trocar (150 mm in length; Ethicon Endo-Surgery, Cincinnati, Ohio) was inserted over the guidewire **(Figure 1b)**. A 10-mm offset hysteroscope (length, 10.5 in; Gyrus ACMI) was inserted through the port to visualize the ureter. In each pig, ureteral trauma from dilation was visible, although the ureter remained intact. Laparoscopic instruments up to 5 mm in diameter were passed through the working channel of the hysteroscope. A bariatric suction device was used to clear the ureteral lumen of blood and urine after dilation. The ureter was opened medially with the use of a bariatric hook electrode (Megadyne, Draper, Utah) to allow access to the retroperitoneal space. Using the hook electrode, the retroperitoneal space was developed and the hilar vessels were dissected **(Figure 1c)**. A 5-mm bariatric bipolar sealing device (Ligasure Advance; Covidien, Mansfield, Massachusetts) was used for further dissection and mobilization of the kidney. The lateral attachments were left intact to stabilize the kidney during renal morcellation.

The pig was repositioned in a 60° lateral decubitus position to allow the bowel to fall away from the kidney. A 2/3-mm transabdominal port (Tyco Healthcare, Norwalk, Connecticut) was placed lateral to the nipple line and several centimeters above the umbilicus. A second 2-mm port was placed (Tyco Healthcare) approximately 8 cm caudal to the first port in the left lower quadrant of the abdomen **(Figure 2)**. A 2.9-mm 12° lens (Stryker Endoscopy, Kalamazoo, Michigan) was then passed through the 2/3-mm port, and a 2-mm grasper was passed through the caudal transabdominal port. The renal artery and vein were divided with a bariatric stapling device (Ethicon Endo-Surgery) **(Figure 1d)**. Kidney morcellation was then carried out with the 5-mm bipolar sealing device through the transureteral trocar. The transabdominal grasper and camera were used for improved renal stabilization and visualization during the morcellation process. Morcellated renal fragments were prevented from migrating by leaving the cranial end attached to apical tissue until fragment removal. After morcellation, each renal segment was removed transureterally by using the empty housing of a 12-mm bariatric stapling device to grasp the fragment for removal **(Figure 1e)**. After complete removal of all fragments, the ureteral stump was closed using a laparoscopic suturing device (SR 5 Quick Load; LSI Solutions, Victor, New York). The skin was reapproximated at the abdominal port sites with cyanoacrylate tissue adhesive, and a urinary catheter was left in place for 10 to 14 days postoperatively. The animals were monitored and cared for in the Institutional Animal Care Facility under the direction of the institutional veterinarian until euthanasia on postoperative day 21. Operative data were collected and analyzed postoperatively. The primary surgeon assessed the technical aspects of each step of the operation to determine the most challenging part of each surgery.

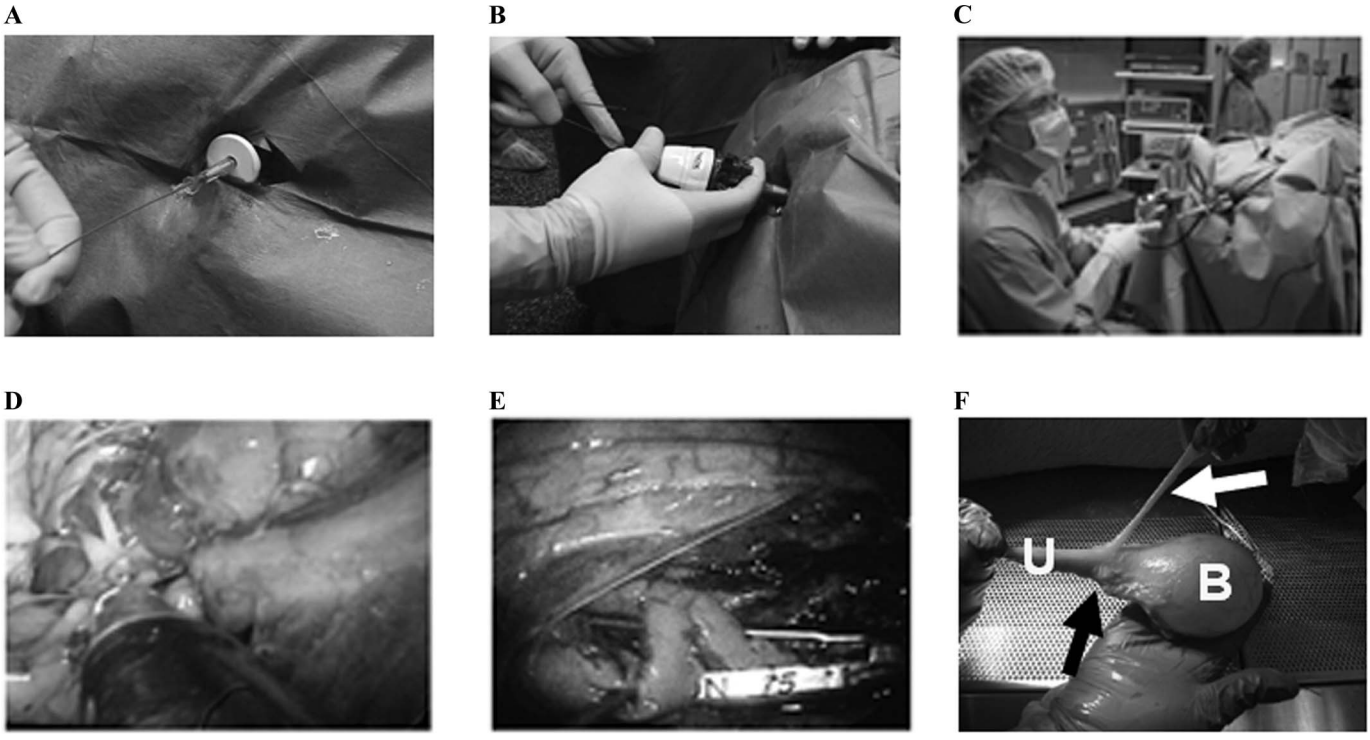

Figure 1. (a) In lithotomy, a superstiff guidewire is placed and used to insert an experimental bariatric balloon-dilator sheath combination. (b) After ureteral and urethral dilation, a 12-mm bariatric port is inserted into the distal ureter. (c) A hook electrode is passed through the offset hysteroscope (with 5-mm working channel) for dissection of retroperitoneal space and renal hilum. (d) A 5-mm bariatric stapling device is used to divide the renal artery and vein. (e) After hilar transection, the kidney is morcellated into 9-mm strips with a bipolar device and removed through the ureter using the empty housing of a bariatric stapling device. (f) Bladder removed at necropsy and instilled with water to demonstrate absence of urine leak. B, bladder; U, urethra. White arrow indicates contralateral ureter; black arrow indicates healed ureteral orifice site.

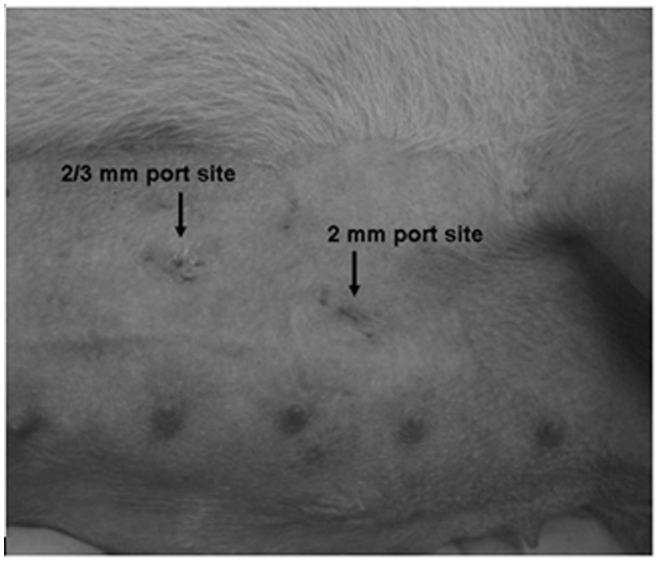

Figure 2. Transabdominal laparoscopic port site.

RESULTS

There were no intraoperative complications in any of the 3 surgical procedures. Mean operative time was 287 minutes. Mean blood loss was 47 mL. One pig developed urinary retention when the Foley catheter became plugged with a clot, which required catheter irrigation. Upon subsequent removal of this catheter, the pig was able to void spontaneously prior to euthanasia with no further complications. The timing of the various steps in the operation and estimated blood loss associated with each operation are shown in **Table 1**. At necropsy, each of the 3 bladders was removed and instilled with saline to test the integrity of the ureteral repair. All bladders were completely healed, without leak at the site of ureteral ligation **(Figure 1f)**. With the exception of the transient clot retention, all 3 pigs displayed normal behavioral patterns and were eating and urinating expected volumes up to the day of euthanasia.

The primary surgeon rated the morcellation portion of the procedure as the most complex in each surgery. The next

Table 1.
Perioperative Outcomes

Variable	Pig 1	Pig 2	Pig 3
Total operative time (min)	232	325	305
Ureteral access	27	40	60
Nephrectomy	98	120	111
Kidney morcellation	107	165	134
Estimated blood loss (mL)	40	25	75
Intraoperative complications	None	None	None
Postoperative complications	None	Clot retention	None

most difficult portion was closure of the ureteral stump. The third most difficult step was the dissection of the retroperitoneum and hilum, because of difficulty maintaining the pneumoretroperitoneum.

DISCUSSION

NOTES is currently in the early stages of development. Yet as technology and surgical innovation continue to progress, NOTES techniques may one day become the procedure of choice for a wide variety of procedures in several different surgical disciplines. Previously, we reported the feasibility of a hybrid transureteral nephrectomy in a nonsurvival porcine model.[8] In the current study, we demonstrate, for the first time, the feasibility of performing a hybrid transureteral NOTES nephrectomy in a survival porcine model. Although 1 of 3 pigs had an episode of acute postoperative urinary retention secondary to a blood clot, there were no other intraoperative or postoperative complications.

Several points of entry into the peritoneal cavity for nephrectomy have been evaluated in animal models,[9–11] whereas only transvaginal nephrectomy has been reported in humans.[12,13] Bazzi et al[14] recently reported successful hybrid transrectal NOTES nephrectomy in 5 female pigs and demonstrated similar outcomes to a transvaginal nephrectomy porcine group. They used a single 12-mm umbilical port during this procedure. They reported an average operative time of 196 minutes, with no evidence of intra-abdominal injuries on necropsy. The authors selected the rectum as the point of entry, citing superior space for the extraction of a large kidney when compared with a transgastric or transvesicle approach, eliminating the challenges of renal morcellation. Transvaginal nephrectomy has been reported using several different surgical techniques. Haber et al[10] reported their experience with a pure transvaginal nephrectomy in 5 female pigs in a nonsurvival model. Dissection was carried out using a needle/knife electrocautery device passed through either a single- or dual-channel videogastroscope. Tissue dissection was aided by retraction supplied by a 60-cm articulated XL EndoGIA stapling device (US Surgical, Norwalk, Connecticut) which was later used for division of the renal vessels. Mean operative time was 113 minutes, and the investigators reported no intraoperative complications. There was no evidence of injury in the intrapelvic cavity on gross examination at necropsy. Using a different approach from pure NOTES transvaginal nephrectomy, Isariyawongse et al[11] published their experience with a combination transvaginal-transgastric technique in a nonsurvival porcine model. After first establishing transgastric access to the peritoneal cavity for passage of a single-lumen gastroscope, a colpotomy was made under direct visualization. A novel transvaginal port was then placed to allow passage of laparoscopic dissection tools as well as a laparoscopic stapling device for division of the hilar vessels and ureter. There were no intraoperative complications. The authors did not detail the closure method, but they did recognize that this was a challenge in the current state of NOTES nephrectomy.

All previously described methods of performing NOTES nephrectomy use novel techniques requiring ingenuity and considerable endoscopic skill. Yet a major limitation is the possible morbidity associated with accessing the peritoneal cavity by intentional viscerotomy of a bacterial colonized hollow viscous. In a randomized-controlled trial, Guarner-Argente et al[15] randomized 40 pigs to standard laparoscopic, transvaginal, transgastric, or transrectal peritoneoscopy. Peritoneal cultures were taken at the completion of the procedure and at necropsy on postoperative day 14. Of concern, they found that all animals had positive peritoneal fluid cultures at necropsy, although no animals exhibited signs of peritoneal infection in the 14-day postoperative study period. The authors concluded that peritoneal contamination occurs regardless of the peritoneal access site; however, it did not lead to septic complications in the porcine model in short-term follow-up. Donatsky et al[16] evaluated a novel technique for obtaining peritoneal access with an ultrasound-guided gastrotomy to accommodate a gastroendoscope for peritoneoscopy. All pigs survived to euthanasia on postoperative day 14, yet 30% (n = 3 of 10) were found to have intra-abdominal abscesses at necropsy. Sotelo et al[12] published one of the first reports of hybrid transvaginal NOTES nephrectomy in 4 patients. In addition to the transvaginal approach, they made a 2.5-cm Z-plasty incision at the umbilicus for placement of a 3-channel R-port

(Triport; Advanced Surgical Concepts, Dublin, Ireland). The first 3 cases required conversion to standard laparoscopy because of rectal injury, difficulty with liver retraction and access to hilar vessels, and inability to adequately control upper pole bleeding in each of the 3 patients, respectively. The fourth case was completed without conversion to standard laparoscopy; however, the patient subsequently developed fever and a fluid collection in the renal fossa that required percutaneous drainage. In a review of 14 cases of hybrid transvaginal NOTES nephrectomy performed at a single center, Alcaraz et al[17] reported that 1 patient developed abdominal pain and fever on postoperative day 2 due to a colon injury, necessitating temporary fecal diversion. In addition to the transvaginal access, the authors used a 5-mm and a 10-mm transabdominal port.

NOTES in animals and hybrid NOTES procedures in humans demonstrate the risks to patients of using a different organ system as the entry site for NOTES surgery. Although designed to minimize morbidity, previously described NOTES techniques violate a fundamental tenet of minimally invasive surgery by intentionally injuring a second organ system. There are few published reports of complication rates in synchronous surgical procedures performed in patients undergoing urologic surgery. However, in a review of 30 patients, Somani et al[18] reported a 15% increase in perioperative morbidity in patients who underwent nephrectomy and a second procedure on a nongenitourinary organ compared with those who underwent nephrectomy alone.

During nephrectomy, the urinary system is violated when the ureter is divided. We report a technique that offers the advantages of a NOTES approach without involving a nongenitourinary hollow viscus by using the ureter to access the abdomen. In the only other technique published in the literature to avoid the violation of a second organ system, Lima et al reported their experience with a pure NOTES transvesical nephrectomy in a nonsurvival porcine model. Using a ureteroscope to create a cystotomy, the surgeon was able to pass a wire transvesically into the peritoneal cavity, which served as a guide for dilation and subsequent passage of a 10-mm operating telescope. One of 6 pigs was noted to have a 1-cm colon laceration at necropsy.

Transvesical nephrectomy confines the procedure to the urinary system but makes a separate opening in a second organ (the bladder) to allow port placement. In contrast, our technique places the entry site through the ureteral orifice to the kidney that is being removed, avoiding the morbidity of a separate opening in the bladder. Most transvesical NOTES procedures place the entry point to the peritoneal cavity in the dome of the bladder; a leak at this site would result in urinary ascites and significant patient morbidity. In contrast, the transureteral approach has the exit of the bladder located in the retroperitoneal space, thereby potentially reducing the morbidity of a urinary leak should it occur.

In an effort to avoid a viscerotomy in a second organ system, we have developed a technique to access the retroperitoneum transureterally. From our perspective, this is a logical application of NOTES surgery to remove the diseased organ through its own natural orifice. A gastrointestinal surgical correlate would be to remove the appendix internally from the colon or to remove the gallbladder through the cystic duct. Although these operations may seem prohibitively complex at the current time when using conventional technology, downsizing of instrumentation and development of new instruments will certainly make these techniques feasible in the future.

Although transureteral nephrectomy theoretically decreases the risk for bacterial contamination of the abdominal cavity compared with a transenteric or transvaginal approach, it does have certain limitations. First, our technique requires morcellation of the kidney for removal via the ureteral access point. This would make this technique less desirable in patients with malignancy because of the risk for possible tumor spillage into the retroperitoneal space. Additionally, this was a time-consuming and challenging portion of the surgical procedure. However, with experience, we anticipate improved efficiency. In addition, the development of a closed system that could be deployed to isolate the kidney and allow morcellation without leakage of cells into the peritoneal cavity could allow transureteral nephrectomy to be used in oncologic applications. Second, the retroperitoneal space is limited in size, making dissection and adequate visualization challenging. A third challenge is the limitation of currently available instrumentation. Despite using the longest prototype bariatric instruments available, it was difficult to access and dissect the upper pole, even in the juvenile female pigs used in this study. Development of longer instrumentation could solve this problem. In addition, the development of an effective bariatric-length 5-mm morcellation device could simplify the procedure. Similarly, the development of a small caliber 3- to 5-mm device that reliably seals the renal hilum would allow the downsizing of instrumentation in general. Finally, this procedure would likely be more easily applied to female patients in its current state of development. The female urethra is

shorter and more accommodating of instruments that are necessary to access the retroperitoneum transureterally. To accommodate these same instruments, the male urethra would likely require an undesirable degree of dilation. Miniaturization of surgical instruments would likely address this shortcoming, potentially making this surgery feasible in the male population. In addition, the use of these smaller caliber instruments (<5 mm) would not dilate the ureteral orifice and ureter as much, potentially eliminating the need for challenging ureteral closure.

CONCLUSIONS

We have demonstrated for the first time the feasibility of performing a transureteral hybrid NOTES nephrectomy in a survival porcine model. This technique represents a novel technique that eliminates the risks associated with the intentional perforation of a separate organ system. However, its practical application in the human population is limited by a current lack of adequate instrumentation. With modification of techniques and development of new instrumentation, NOTES procedures limited to a single organ system could alter how many surgical procedures are performed. Once fully developed, single-organ-system NOTES surgery could further reduce patient morbidity and represent the next surgical paradigm.

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